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75	90 01/21/2004		EXAM	INER	
VICTORIA L. BOYD			RAO, MANJUNATH N		
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Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)			
Office Action Summary		10/028,245	DUNN-COLEMAN ET AL.			
		Examiner	Art Unit			
i i		Manjunath N. Rao, Ph.D.	1652			
The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply						
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). Status						
	Responsive to communication(s) filed on <u>07 N</u>	ovember 2003.				
·		action is non-final.				
3)	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.					
Dispositi	on of Claims	÷				
4)🖂	Claim(s) <u>1-17,19,20,22-24 and 26</u> is/are pendi	ng in the application.				
	4a) Of the above claim(s) is/are withdrawn from consideration.					
5)⊠	Claim(s) 23 and 24 is/are allowed.					
	Claim(s) <u>1-17,19,20,22 and 26</u> is/are rejected.					
	Claim(s) is/are objected to.					
8)∐	Claim(s) are subject to restriction and/or	r election requirement.				
Application	on Papers		•			
9) The specification is objected to by the Examiner.						
10) The drawing(s) filed on is/are: a) □ accepted or b) □ objected to by the Examiner.						
	Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).					
	Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).					
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.						
	nder 35 U.S.C. §§ 119 and 120					
 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: 1. Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. 						
13)∭ A sir 37	cknowledgment is made of a claim for domestic nce a specific reference was included in the firs CFR 1.78. The translation of the foreign language pro	c priority under 35 U.S.C. § 119(est sentence of the specification or	e) (to a provisional application) in an Application Data Sheet.			
14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.						
Attachment	(s)	*				
1) 🔀 Notice 2) 🔲 Notice	of References Cited (PTO-892) of Draftsperson's Patent Drawing Review (PTO-948) ation Disclosure Statement(s) (PTO-1449) Paper No(s)	5) Notice of Informal Pa	(PTO-413) Paper No(s) atent Application (PTO-152)			

Art Unit: 1652

DETAILED ACTION

Claims 1-17, 19-20, 22-24 and 26 are now currently pending in this application and are under consideration.

Applicant's amendments and arguments filed on 11-7-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically, Examiner has withdrawn the rejections under 35 U.S.C. 112, 2nd paragraph in view of claim amendments. In that regard please see the enclosed page from the English language dictionary.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete <u>all</u> the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 and claims 3-17, 19-20 that depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 2 is drawn to a polynucleotide selected from a group of different polynucleotides. However, in parts (a) and (b), the polynucleotide is referred to as encoding a polypeptide having a certain % sequence identity to

Art Unit: 1652

the amino acid sequence presented in "Figure 2 (SEQ ID NO:2)". This recitation is confusing. This is because it is not clear whether said polypeptide specifically has the amino acid sequence with SEQ ID NO:2 or to that represented in figure 2. The recitation indicated above is confusing because it gives an impression to those skilled in the art that the amino acid sequence represented in figure 2 is the same as the amino acid sequence SEQ ID NO:2. Furthermore, a perusal of figure 2 and its description indicates the sequence as having both SEQ ID NO:2 and SEQ ID NO:3 without indicating as to where SEQ ID NO:2 starts and ends, which adds to the confusion. In their response to the previous objection by the Examiner, applicants have traversed the objection arguing that the sequences represented in figure 2 and SEQ ID NO:2 are different. Therefore claim 2 and claims depending therefrom continues to be indefinite.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 19-20, 22, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide isolated from *T.reesei*, with SEQ ID NO:1 or 4 encoding a polypeptide with SEQ ID NO:2 having endoglucanase, (EGVIII), activity and a method of making said endoglucanase, by transforming a host cell with an expression vector comprising the polynucleotide with SEQ ID NO:1 or 4 followed by cultivating the host cells and recovering the expressed endoglucanase, and being enabling for a recombinant host cell in which the polynucleotide with SEQ ID NO:1, 4 has been inactivated such that it does not express a functional endoglucanase, does not reasonably provide enablement for such a

Art Unit: 1652

polynucleotide isolated from any fungi, or a polynucleotide encoding polypeptides with endoglucanase activity, and having 85%, 90%, or 95% sequence identity to SEQ ID NO:2 or such polynucleotides that hybridize under intermediate to high stringency conditions to a probe (of any length) designed to hybridize with the nucleotide sequence disclosed in figure 1, vectors and host cells comprising such polynucleotides, and a method of making said encoded endoglucanase, by transforming a host cell with an expression vector comprising the said polynucleotides followed by cultivating the host cells and recovering the expressed endoglucanase, or a recombinant host cell which does not express a functional endoglucanase, of any fungi. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-17, 19-20, 22, 26 are so broad as to encompass any polynucleotide from any fungal source encoding an endoglucanase, vectors host cells and methods of expressing said endoglucanase and a recombinant host cell in which the polynucleotide encoding the endoglucanase is inactivated. Claims are also so broad because they encompass any variant or mutant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to

Art Unit: 1652

SEQ ID NO:2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims.

Claim 1 is drawn to any polynucleotide encoding any endoglucanase (even though applicants coin the term EGVIII) from any or all fungal source. Fungi are a large group of microorganisms including several hundreds and thousands of members. They are also highly varied in their nutrition requirements and growth conditions. Applicants have provided support in their specification for isolation of a polynucleotide encoding an endoglucanase only from a single fungal source. Applicants have not taught a universal method of isolation and characterization of polynucleotides encoding endoglucanases from any fungal member. While methods to cultivate a good number of fungi are well known in the art, there is no universal single method for cultivating, testing and isolating endoglucanase from any or all fungal species. As stated earlier, members of the fungi group are diverse with varied nutritional and growth requirements. Therefore, it would be undue experimentation for those skilled in the art to test each and every fungal species for polynucleotides encoding endoglucanase using the method provided by the applicants which applies to only a single fungal species, *Trichoderma*. Applicants have not shown that the method they have used for isolation of the polynucleotide from Trichoderma can be successfully used for each and every fungi that are known and unknown to man.

On similar lines, while applicants have provided SEQ ID NO:1 and 4 and host cells comprising such polynucleotides, and those skilled in the art would be enabled to inhibit such host cells from expressing endoglucanse encoded by SEQ ID NO:1 or 4 by going in and making

Art Unit: 1652

changes to SEQ ID NO:1 or 4 they have not provided methods to do the same with host cells expressing any fungal endoglucanase because applicants have not provided methods to isolate such polynucleotides in the first place. Therefore without such polynucleotides, those skilled in the art would be unable to make host cells containing such polynucleotides in the first place. Furthermore, applicants have also not taught a universal method that can be used to inactivate any fungal polynucleotide encoding endoglucanase in any host cell. Therefore claims drawn to host cells in which polynucleotides encoding endoglucanase are inactivated remain non-enabled.

With respect to claims directed to variant polynucleotides encoding polypeptides that have 85%, 90%, or 95% sequence identity to SEO ID NO:2, applicants have not taught those skilled in the art as to how to make and select the claimed polynucleotides, which leads to undue experimentation for those skilled in the art. Since the amino acid sequence of a protein encoded by a given polynucleotide, determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity, requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant to modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single endoglucanase, obtained from T. reesei and having an amino acid sequence SEQ ID NO:2. Putting it in simpler terms, the specification is silent regarding the specific amino acids or specific regions in the amino acid sequence of SEO ID NO:2 that can be modified (by insertion, deletion or substitution) without affecting the endoglucanase activity which could be used to construct variant polynucleotides. Therefore, it would require undue

Page 7

Art Unit: 1652

experimentation by a skilled artisan to identify such regions that can be changed and make and use all the claimed variant polynucleotides. The specification is limited to teaching the use of just SEQ ID NO:1 or 4 as polynucleotides encoding the polypeptide with SEQ ID NO:2. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of a universal method of isolating polynucleotides encoding an endoglucanase from any fungi and lack of guidance regarding where to make the changes in the polypeptide/nucleotide sequences, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892) to make a polynucleotide sequence, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass polynucleotides encoding endoglucanase from any or fungi, polynucleotide encompassing any or

Art Unit: 1652

all modifications and fragments encoding a polypeptide with 85%, 90%, or 95% identity to the SEQ ID NO:2 or polynucleotides that hybridize under intermediate to high stringency conditions to a probe (of any length or function) designed to hybridize to the polynucleotide with SEQ ID NO:1, because the specification does not establish: (A) a single universal method to isolate polynucleotides encoding endoglucanse from any fungi; (B) a single universal method to inactivate polynucleotides encoding endoglucanse from any fungi in any host cell; (C)regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional endoglucanase; (D) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any nucleotide in any fungal polynucleotide with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides from any fungi or polynucleotides with an enormous number of modifications of to the polynucleotide encoding the amino acid with SEQ ID NO:2 (SEQ ID NOS:1 or 4). The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Art Unit: 1652

In response to the previous Office action, applicants have traversed the above rejection. Applicant argues that because the court overturned the enablement rejection in one specific case (In re Dinh-Hguyen, 181 USPQ 46(CCPA 1974)), the instant enablement rejection must be withdrawn as the situation in the instant case is similar to the case involved in the above court ruling. Examiner is not aware of the claims involved, claim language and the prosecution history of the above case and is therefore unable to concur with the applicant. Applicant also alleges that Examiner is merely objecting to "extremely large number of polynucleotides" which is insufficient (to reject the claims under enablement) and is an unsupported conjectural statement. Examiner respectfully disagrees with such a misplaced argument. Indeed applicant's claims are directed to extremely large number of polynucleotides. Applicant is claiming any or all polynucleotides encoding endoglucanse literally from any or all fungi. Added to that, applicant claims polynucleotides that encode polypeptides that are 85%, 90%, and 95% identical SEQ ID NO:2. A simple mathematical calculation would indicate those skilled in the art that this amounts to an "extremely large number of polynucleotides" not supported by the applicant's specification. Applicant appears to conclude that merely naming the encoded endoglucanse as EGVIII overcomes all the issues related to breadth and enablement of the claims involved. Examiner would like to reiterate that he has analyzed the claims not based on "conjecture" but based on the "Wands factors" and scientific facts. With respect to variant polynucleotides applicant's arguments are not persuasive because while methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants requires that one of ordinary skill in the art be provided with guidance for making specific changes and for the selection of which of

Art Unit: 1652

the large number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) a single universal method to isolate polynucleotides encoding endoglucanse from any fungi; (B) a single universal method to inactivate polynucleotides encoding endoglucanse from any fungi in any host cell; (C)regions in the polynucleotide structure which may be modified without effecting its activity of encoding a functional endoglucanase, EGVIII; (D) the general tolerance of said polynucleotide sequence to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any nucleotide in any fungal polynucleotide with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Claims 1, 6-7, 19-20 22 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding fungal endoglucanase, and a method of producing

Art Unit: 1652

endoglucanase, using DNA molecules encoding any fungal endoglucanase in a *Aspergillus* host cell.

The specification does not contain any disclosure of the structure of all DNA sequences that are encompassed by the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicant has not provided any argument against the above rejection. However, as the claims continue to lack written description, Examiner has maintained the above rejection.

Examiner has withdrawn the rejection of claims 8-9 and 11 under 35 U.S.C. 112, Ist paragraph for lack of written description in view of the claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-7, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhikhabhai et al., 1984, J. Appl. Biochem., Vol. 6:336-345, cited in the IDS) and Okada et al. (Appl. Environ. Microbiol., 1998, Vol. 64(2):555-563). This rejection is based upon the public availability of printed publications. Claims 1, 6-7, of the instant application are drawn to an isolated polynucleotide derived from a fungal source encoding an endoglucanase (which applicant calls EGVIII) (claim 1), said polynucleotide isolated from a *Trichoderma* source such as *T.reesei* (claims 6-7).

Bhikhabhai et al. teach the isolation of two endoglucanases from a *T. reesei* source. However, Bhikhabhai et al. call the two endoglucanases as endo II and endo III one of which has almost the same molecular weight as that of the instantly claimed endoglucanse. However, the reference does not teach either the amino acid sequence or the polynucleotide sequence encoding the enzymes. Based on the identical source and almost identical molecular weight and identical activity of the reference polypeptide and polypeptide encoded by the claimed polynucleotides, Examiner takes the position that the enzyme in the reference and that disclosed in the instant application are inherently one and the same. The only difference Examiner sees between the enzyme in the reference and the instant disclosed enzyme is that applicant calls the enzyme as EGVIII, while the authors of the reference call the enzyme as endo II or endo III. Except for the different names Examiner sees no other difference between the two enzymes. (Since the Office does not have the facilities for examining and comparing applicants' protein

Art Unit: 1652

with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.)

Okada et al. teach methods to obtain a polynucleotide, encoding an endoglucanase, isolated from a *Trichoderma reesei* using recombinant technology. The reference also teaches methods to isolate RNA molecule, and construct an expression vector comprising said polynucleotide. (However, it should be noted that at the time this instant application was filed, methods to obtain the amino acid sequence of purified proteins were very well known and established in the art. Furthermore, methods to obtain or deduce polynucleotide sequence encoding the proteins whose amino acid sequences were known was also well established in the art)

Therefore, combining the teachings of the above two references, it would have been obvious to those skilled in the art to take the purified endoglucanase from Bhikhabhai et al. use the methods taught by Okada et al. and obtain the polynucleotide encoding the endoglucanase and name the encoded recombinant enzyme as EGVIII. One of ordinary skill in the art would have been motivated to do so in order to make expression vectors for expression and production of the encoded enzyme using industrial host cells. One of ordinary skill in the art would have a reasonable expectation of success since Okada et al. teach successful methods for doing the same.

Art Unit: 1652

Therefore, the above claims would have been *prima facie* obvious to those skilled in the art.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bhikhabhai et al., Okada et al. (see above) and Ward et al. (US 6265204, 7-2001). Claim 26 is drawn to a method of expressing a heterologous polypeptide having endoglucanase activity in an *Aspergillus* species by transforming a *Aspergillus* host cell with an expression vector comprising a polynucleotide encoding a signal sequence linked to a polynucleotide encoding a heterologous endoglucanase encoding a chimeric polypeptide followed by cultivating said host cell such that the chimeric polypeptide is produced.

Bhikhabhai et al. teach the isolation of the endoglucanase enzyme from *T. reesei* (see above).

Okada et al. teach a polynucleotide isolated from *Trichoderma sp.* encoding a polypeptide with endoglucanase activity. However, the reference does not teach the production of the same in a *Aspergillus* host cell as a chimeric polypeptide linked to a heterologous signal peptide sequence.

Combining the teachings of Bhikhabhai et al. and Okada et al. it would have been obvious to those skilled in the art to arrive at polynucleotide sequence encoding the endoglucanase with or without its own signal peptide. However, the teachings of both the above reference does not indicate the use of *Aspergillus* host cell and its advantages for expressing the above polynucleotide.

. 1650

Art Unit: 1652

Ward et al. teach methods of preparing expression constructs comprising heterologous signal peptide sequence for secretion of heterologous polypeptide in filamentous fungal host cells such as *Aspergillus*. Ward et al. teach that filamentous fungal host cells make ideal hosts for expressing heterologous polypeptides and provides the reasons for the same

With the above three references in hand, it would have been obvious to those skilled in the art to use the polynucleotide sequence obtained from *Trichoderma sp.* encoding a endoglucanase by the combination of Bhikhabhai et al. and Okada et al. and introduce such polynucleotides into vectors provided by Ward et al. and express the same in filamentous fungal host cells such as *Aspergillus*. One of ordinary skill in the art would have been motivated to do so as Ward et al. teach that filamentous fungus host cells secrete the polypeptide into the culture medium thereby making it easy for isolation of expressed polypeptide. One of ordinary skill in the art would have a reasonable expectation of success since the combination of Bhikhabhai et al. and Okada et al. provides the polynucleotide encoding an endoglucanase and Ward et al. provide vector and host cells to express the endoglucanase in *Aspergillus*.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

Conclusion

None of the claims except 23-24 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1652

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

Manjunath N. Rao January 16, 2004